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cacatga 127

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A method of inhibiting off-target cleavage of a DNA molecule by a first guide RNA-endonuclease complex, wherein the first guide RNA-endonuclease complex comprises a first guide RNA comprising a nucleotide target recognition sequence complementary to a first target sequence, the method comprising:

contacting the DNA molecule with a second guide RNA-endonuclease complex, wherein the second guide RNA-endonuclease complex comprises a second guide RNA comprising a nucleotide target recognition sequence with 16 or fewer nucleotides and is complementary to a second target sequence in the DNA molecule, wherein the second target sequence is different from the first target sequence but the second target sequence is capable of cleavage at a measurable rate by the first guide RNA-endonuclease complex.

2. The method of claim **1**, further comprising contacting the DNA molecule with the first guide RNA-endonuclease complex, and wherein second guide RNA-endonuclease complex is contacted to the DNA molecule prior to or simultaneously with the first guide RNA-endonuclease complex.

3. The method of claim **2**, wherein the first guide RNA-endonuclease complex and the second guide RNA-endonuclease complex are contacted to the DNA molecule at a ratio of about 20:1 to about 1:20.

4. The method of claim **1**, wherein the second target sequence differs from the first target sequence by 0-10 nucleotide mismatches.

5. The method of claim **1**, wherein the first guide RNA-endonuclease complex comprises a first endonuclease and